[ъ]~<S

The differentiation of distinct cell types from protocells can be corresponded to the expression of cell fate~<0>~determining transcription factors in progenitor cells.

Transcription factors impact the accessibility of different cell states and are dynamically modified during cell differentiation giving rise to a cell-type specific landscapes which in turn modulate the expression of transcriptional factors important for cell identity and functions.

Development processes can be characterized by transient expression of certain genes at specific times.

Cells are characterized in terms of their progression through a dynamic process according to their <gene>~expression patterns.

Ongoing lineages continuously produce local variations that take time and essentials to spread over the populated area: ~<arr|sed>~ in the center of large compact areas have the higher chance to spread.

Cell lines can be expressed in terms of their progression through the dynamic process and can be corresponded to a/the patterns of [a/the] <gene>_expression~s;

In neuronal lineage, particular subtypes of fully differentiated neurons and glia cells are arrived at as a result of sequential expression of such positional markers and ~<fate0determining>~ genes.

Nuclear Factor One (NFI) transcription factors are essential for astrocytic differentiation from progenitor cells into various differentiated cell populations.

Nuclear factor one proteins [<NFIA>|<NFIB>|<NFIC>|<NFIX>] constitute a family of dimeric DNA-binding proteins with very similar DNA-binding specificity and functions, acting as cellular transcription factors with diversity of the protein family generated by multiple genes, differential splicing and/or heterodimerization. During development transcriptional factors are expressed in progenitor cells that give rise to various differentiated cell populations in the dorsal telencephalon, their expression drives the differentiation, <NFIA> and <NFIB> expression persist in mature astrocytes. Overexpression of these genes are sufficient to rapidly convert induced pluripotent stem cells into functional astrocytes *in vitro*.

Astrocytes represent one of the most abundant cell types in central nervous system and are able to dynamically control a broad range of structural and/or functional properties in human brain: formation of the blood barrier, metabolic and trophic support, synaptogenesis and synaptic pruning, neurotransmitter uptake, ionic milieu control in the extracellular space, innate and adaptive immunity, neural repair to name a few.

Characterized emergence of neural diversity in the embryonic spinal cord revealed [set] of transcriptional factors that further partition all major neuronal subtypes. The onset of expression of these different chords occurs at characteristic timepoints during the neurogenic period of spinal cord development. In all observed domains, the earliest neurons express [<Pou2f2>|<Zfhx2>], while later born neurons express [<NFIA>~<NFIB>~<NFIX>] and [<Neurode2>~<Neurode6>], where [<Neurode2>~<Neurode6>] is able to control neuropeptide expression in inhibitory neurons in the dorsal horns of the spinal cord at least; <Pou2f2>|<Zfhx3>|[NIF]~s able to define distinct

subpopulation on <Pitx3>_positive neurons born from the midbrain floor plane, including dopaminergic neurons.

Retinal Ganglion Cells are the first characterized neuronal cell type in the developing retina of vertebrates. Pro-astroglia transcription factors <Sox9>|<NFIA>|<NFIB> strongly expressed from day 14 onward, by day 30 more than 85% of total cells express <NFIA>.

During central nervous system development, early neuroepithelial cells give rise to retinal ganglia cells, generating array of neurons in the cortical plane, providing scaffold for migratory neurons (neurogenic phase). Cells that remain proliferative through the progressive waves of neurogenesis, subsequently differentiate into astrocytes and then latter transition into oligodendrocytes (gliogenis phase). The invariance of these developmental sequence: neurogenesis followed by gliogenesis is highly conserved throughout vertebrate phylogeny. Retinal Ganglion Cells (RGS) can be directly differentiated into astrocytes without going through a neurogenic phase by forced expression of <NFIA>.

The [<NFIA>|<NFIB>|<NFIC>|<NFIX>] family of transcription factors express enriched expression in retinal progenitor cells where they are act as regulators of bipolar interneuron and glia specification, providing a switch to [~<a/the>~] proliferative quiescence.

Proliferative quiescence (also referred to as [G0] stage in the cell cycle) is the cell state defined by temporary and reversible absence from proliferation. Quiescence can be seen as a reversible arrest of proliferation, where quiescent cells able to exit the [G0] stage and resume proliferation upon appropriate stimuli;

In general, neural progenitor cells of the developing central nervous system during course of neurogenesis undergo stereotypical, stage dependent transition including:

I. Initial transition from slowly proliferating, relatively quiescent neuroepithelial cell status into actively proliferating neurogenic progenitors;
II. A progressive transition of neural progenitor cells from symmetric proliferation to asymmetric self-renewing divisions;
III. Letter transition into terminal neurogenic divisions: changes in developmental competence or the ability of neural progenitor cells to give rise for different subtypes of neurons and glia;

An available data indicates substantial sharing of transcription factor regulated gene expression programs amongst glia cells achieved by decomposition of these programs into overlapping modules. A similar relationship was true for modules associated with astrocytes and epithelial glial cells.

Observed synchronized transcription factors expression and motif activity for dynamic regulators along neuronal developmental pseudotime indicates cohesive, sequential, waves of activations during human genesis, consistent across gestation time points:

i. Early activity motifs: <Sox>|<GLI>|<Pax>, exhibiting moderate synergies;
ii. Intermediate activity motifs: <EOMES>|<TBX>|[NFI]~s that are highly synergetic within their class;
iii. Late activity motifs: <NEUROD2>|<BHLHE22>|<MEF2> that are less cooperative and generally appear to operate more independently;

Waves of gene regulation by key transcription factors across a nearly continuous differentiation trajectory into <glutamate>|~<ergic neurons, distinguishing the expression programs of glial lineages and identities lineage-determining transcriptional factors that exhibit strong correlation between linked <gene>~|regulator| elements and their expression levels. These highly connected genes adopt an active chromatin state in early differentiating cells, consistent with lineage commitments.

The genome-wide chromatin accessibility differences between primary neural stem and progenitor cells in quiescent and activated states indicates that distinct cellular states exhibit both shared and unique chromatin profiles, both associated with gene regulation. The accessible chromatin profiles specific to quiescent or activated cells are active enhancers bound by pro-neurogenic quiescence factors <ASCL1> and [NFI]~s. In contrast, shared states are gene promoters harboring constitutively accessible chromatin states enriched for particular core promoter elements that are functionally associated with translation and metabolic functions. Distal active enhancers profile highly enriched for binding of transcriptional regulators of quiescence and activation <NFIX> and <ASCL1>, whereas stable chromatin regions express enrichment in <CTCF> motifs, a known insulator.

The available data indicates that early cortical areal patterning is influenced by strong, mutually exclusive frontal and occipital gene expression signatures, with resulting gradient giving rise to the specification of areas between these two poles throughout successive developmental timepoints, subdividing a human brain into distinct anatomical structures where early morphogenic gradients are help to establish an early blueprint for the specification of brain regions and cortical areas.

Gradients seeded up at particular developmental stage provide specific information about location, resulting in reference pattern formation. The gene expression patterns provide base for cellular lineages and can be locked in place by persistent expression of specific genes.

Structure can develop by assortative mating without any additional drivers subsequently creating a structured population where relatively homogeneous regions separated by distinct clines.

Diffusional flow alone can lead to homogenization of all populations;

The combination of diffusion and ongoing lineages results in isolation by distance where differences between local populations increases with distance. The magnitude of these differences/clines depends on the balance between diffusion and mutation rates.

Large migration sweeps emanate from the central regions of large compact areas and spread towards the margins result in remarkably consistency of directions, quite independent from [a/the]~<parameter>~ settings.

Hematopoiesis: <hematopoietic>~[stem]~<cells~differentiat>:<S | give rise to developed blood cells belonging to ~<myeloid>~[or]~<lymphoid>~ lineages. In human embryo, definitive blood stem cells first observed in the aorta region at 4-5th post conception weeks. Hematopoiesis as the process then migrates to the fetal liver region and subsequently to the bone marrow tissue, which becomes a dominant hematopoietic organ at birth and remains so through a life. Hematopoietic differentiations have been metaphorically represented as linear trajectories with discreate steps from hematopoietic stem cells to matured cell types. Measurements of cell-to-cell variability among cells at the same stage of differentiation indicates a transient peak of expression variability in all of the differentiation pathways; genes with highest entropy variation for a given differentiation pathway corresponds to pathway-specific genes, whereas genes with the highest expression variation common to all pathways.

Transition between states can be corresponded to the presence of small [set] of ruderal symbionts that are rare in mature system but can act as keystone mutualists.

Difference between alternative states can be directly linked to ~{biom}~ symbioses and mostly independent from initial conditions.

Mechanically quite similar to biologically described method of nitrogen fixation in plants: Although molecular nitrogen [N~N] is abundant in the atmosphere, plants cannot directly access the form of nitrogen. Biological nitrogen fixation is an essential process that transforms atmospheric nitrogen into ammonia – form of nitrogen that is biologically useful for plants. Nitrogen limitation in soils can be seen as an essential evolutionary constraint. As a result, plants have developed multiple strategies allowing them to associate with nitrogen fixing bacteria in order to procure better nutrition. Plant-bacteria interactions have been relatively well studied in legumes, which can symbiotically associate with a phylogenetically diverse group of bacteria, collectively called *rhizobia*, in a species-specific manner. Symbiosis is established by activation in plant signal-transduction pathway, which include two families of genes called [Nodulation Signaling Pathway] and [Nodule Inception] genes, activated in the presence of environmental factors secreted by bacteria's and under nitrogen limited condition; genes code for transcription factors, regulators of bacteria symbionts establishment and nodule organogenesis. Symbiotic establishment by *rhizobia* into legume roots leads to the formation of a specialized organ known as root nodule in which *rhizobia* differentiates into nitrogen-fixing symbionts. In exchange for atmospheric nitrogen fixed by symbionts, legumes provide energy and carbon sources to the bacterial partner; root nodules not only create an optimized environment for nitrogen fixation, but also provide a site where substance exchange can take place. Plants recruit beneficial microorganisms dynamically and selectively using root modules rich in organic compounds, amino acids and/or organic sub-compounds with multiple molecules abele to be involved in the recruitment process. Microorganisms present diverse apparatus for compound transitions: as biomass turns over through a time beneficial compounds become available to plants.

The scRNA-Seq (Single ~{cell}~ RNA Sequencing) profile for human embryos cervical and thoracic regions in Carnegie Stages (CS) reveal the transcriptome of progenitor and neuronal populations from neural tube as well as cells adjacent to the neural tube; indicating dozens of distinct cell types and facilitation in reconstruction of the differentiation pathways for specific neuronal subtypes;

An analysis of the sequential expression of gliogenic markers in progenitor cells:

- <Sox9> was detected at low levels across progenitor domains from CS12, followed by the detection of [<NFIA>~<NFIB>] at CS17 at higher levels in ventral progenitors with increase of expression in dorsal progenitors by CS19;
- The expression of <Sox9> and [<NFIA>~<NFIB>] in progenitors and neurons is similar to emmunohistochemical assays of the embryonic human spinal cord;
- The expression of <NFIA> correlates with the onset of ~|glioginesis|~ and is observer at CS15 in ventral progenitors and delayed until CS18 in dorsal regions;

Analysis of scRNA-seq data indicates: during the earliest events in human hematopoietic stem cells differentiation, changes can be characterized by only subtile molecular changes in continuum of low-primed cell states with hematopoietic stem cells and progenitor cells exist as a gradually transition into a specific lineage~s.

The transforming growth factor beta (TGF*b*) signaling pathway involved in processes: cell growth, cell differentiation, cell migration, apoptosis, cellular homeostasis; the signaling pathway are evolutionary conserved trait. The mechanical process can be described as a relatively simple process: the TGF*b* ligands bind to a [type||] receptor, which recruits and phosphorylates a [type|] receptor. The [type|] receptor then phosphorylates receptor-regulate<SMAD>~s R-SMAD which can now bind the <SMAD4> ~coSMAD. [R-SMAD~coSMAD] complexes accumulate in the nucleus where they act as transcription factors and participate in the regulation of the gene expression. TGF*b* signaling can be corresponded to the timing of developmental temporal switches in nervous system and promotes the expression of the late progenitor marker <NFIA> in neurogenic stem cell lines.

<NFIA> and <NFIB> shown activities required for the generation of late neuronal subtypes, with <NFIB> overexpression linked to increase in chromatin accessibility, promote expression of pro-metastatic genes, possible as downstream target of <cMYC>, which directly regulates its expression, contributing to rapid metastatic formation.

<NFIB> regulates [set of 60 genes] in the sub translational regulatory network for adolescence and is essential for late forebrain development, where loss of <NFIB> gene leads to defects in basilar pons formation and hippocampus development.

The <NFIA> and <NFIB> genes can be corresponded to positions <1.p31.2-1p.31.3> and <9p24.1> respectively. The <NFIC> and <NFIX> genes both can be localized to position <19p.13.3> in the order [centromere]~<NFIX>~<NFIC>~[telomere]. Comparison of the position of [<NFIA>|<NFIB>|<NFIC>|<NFIX>] genes and <JUN> genes suggest a possibility of a close physical linkage between members.

The [Hall] effect occurs in conducting materials when force acts on a charge current in the presence of a magnetic field.

For the models with the smallest ground-state degeneracy, thermal fluctuations select a particular subset of ground states, where the interactions with surrounding units [~] is fixed by a self-consistency condition.

The valley degree of freedom can be distinguished in systems where inversion symmetry is broken. Under a small inversion symmetry-breaking potential a ~{curvature}~ is sharply peaked. If the inversion symmetry-breaking potential increases a ~{curvature}~ is sharply peaked. If the inversion symmetry-breaking potential increases a ~{curvature}~ pertaining to each valley can be broadened and partially mixed with each other.

In a frame of [spin~orbit] interactions seen as highly nontrivial topological systems, named topological insulators. Spin and orbital degrees of freedom can exhibit a simultaneous glass transition, working as dynamical disorder for each other. Randomness induces spins for zero- or finite- temperature objects. The interplay of spins and orbitals is mediated by lattice distortions that select the choices of orbitals, which then generates variant spin exchange interactions raging from magnetic to antimagnetic ones. Antiferomagnetic order coupled to the valley degree of freedom results in a [spin~valley] degree of freedom, leading to [spin~valley]-depended selection rule under strong enough coupling.

In the context of magnetism phenomenon, can be observed in triangular of tetrahedral [unit**X**based] lattice structures with antiferromagnetic interactions as a geometric frustration, preventing the magnetic moments (spins) from pointing antiparallel to each other, resulting in critical modes with no unique preferred state chosen at given critical condition; as a consequence, a system exhibits a propensity for [~] | thermal and/or quantum fluctuations around equilibrium point.

Antisymmetric interactions influence a formation of topological abnormalities. The live>~<time asymmetry is depended on [~]frequency, the higher a frequency more pronounce it is.

The resulting equilibrium point renders dissociation and association rates for given aggregate size assembly in addition to non-equilibrium mechanisms that can modify <association/dissociation> rates of the/a stable finite size aggregates.

All observed living carbon organisms have evolved to contain a [set] of proteins with variable physical and chemical properties. Most of self-replicating living species can be characterized by the presence of [genome]~<able to produce>~:[set of proteins];

The diversity of living entities, from unicellular organisms to mammals can be corresponded to varying repertoire of proteins.

Ribosomes are ubiquitously produced organelles expressed in all cells and tissues, [ribosome]|s: are macromolecular complexes able to catalyze protein synthesis during protein synthesis in all observed living cells according to corresponded genetic information variations. rRNA a component of [ribosome]| the environmental factor for <tRNA>~<mRNA> translation;

Ribosomal proteins genes encode structural components of ribosomes.

In eukaryotes, each ribosome consists of two subunits, the <small> subunit and <large> subunit, corresponded to different ribosomal proteins in addition to different types of ribosomal RNAs:

mRNA – Messenger RNA: corresponds to amino acid sequence of a polypeptide;

tRNA – Transfer RNA: transfers amino acids to [ribosome] during translation;

rRNA – Ribosomal RNA: in addition to ribosomal proteins, makes up the [ribosome]|s the organelles that translate mRNA;

snRNA – Small nuclear RNA: with proteins forms complexes that are involved in RNA processing in eukaryotes (not observed in prokaryotes;
,

A [Proteome set] guide the morphology and functionality of an organism.

A proteome [set of Ribosomal Proteins] are highly conserved in all observed carbon domains of life. Each ribosomal protein (RP) can be corresponded to unique amino acid sequence, with very limited to none similarities between members. Genes are expressed at rate limiting levels, rendering their biological functions as highly sensitive to copy-number variations, resulting in genomic instability variations;

Ribosome assembly consists of both sequential and parallel processing steps. The mixture of sequential and parallel processes provides a rich environment for potential assembly pathways. Under a particular growth condition, ribosome assembly flux can partition between available parallel assembly pathways corresponding to the rates of those pathways, with greater flux along the more rapid assembly pathway. The availability of alternative parallel pathways provides an added degree of robustness to buffer the system against changes in proteins or assembly factors availability variations.

Accessory biogenesis factors help guide the ribosomal assembly process, many of them are nonessential, implying that the reaction they catalyze can be bypassed by alternative pathway|~s. The factors are present and could be necessary under particular environmental conditions. Ribosome profiling experiments in addition to direct quantitative mass spectrometry measures indicate that the assembly factors are up to 5% of total ribosome mass.

Ribosomal biogenesis is a process involving three RNA polymerases: [<RNA Polymerase I>~<RNA Polymerase II>~<RNA Polymerase III>] + addition of post/non-ribosomal factors that are requires for the synthesis, process, transportation and assembly of sub-components in pre-ribosomes; the process seen as multistep cycled process:

For given accessory biogenesis factors and snRNAs:

- <47S>/<45S> rRNA synthesized by <RNA Polymerase I>;
- RP-encoding mRNA provided by <RNA Polymerase II>;
- <5S> rRNA generated by <RNA Polymerase III>;
-

Under reach medium growth condition majority of available RNA polymerase clusters actively engage in rRNA transcription: during transcription, RNA copies of DNA genes are synthesized by <RNA Polymerase>~[enzymes]; product is the messenger RNA, coding order of amino-acid needed to be combined to synthesize of a protein.

Messenger RNA is decoded by complex macromolecules – [ribosome] – able to sequentially decodes mRNA to its corresponded amino-acid sequence; the amino-acid peptide is elongated until ribosome reaches a stop codon, detaches from mRNA, form amino-acid-chain/peptide, released as protein.

The key teem players in the process of protein synthesis are <RNA Polymerase>|s and [ribosome]|s capable of self-replicate by jointly producing their sub-components able to self-assemble into new <RNA Polymerase>~s and [ribosome]~s.

Cycles are assembled to yield the <90s> pre-ribosome in the nucleus, which undergo multiple modifications and subsequently separation into pre-<60S> and pre-<40S> particles. During transport from nucleus to the cytoplasm, these pre-ribosomes are dissociated from most of their non-ribosomal factors and able to maturate into [<60S>~<40S>] | [ribosomal] subunits.

A group of ancestral prokaryotic cells were transformed into what now referred to as eukaryotes by acquirerring a DNA storage compartment – the nucleus – that was separated from rest of the organism by a nuclear membrane equipped with selectively penetrable channels named nuclear pores. To assist in passage between organism and nucleus via the nuclear pores, cellular proteins have been evolved each with specialized signal sequences the nuclear localization signals; a typical nuclear localization signal is a short and surface exposed stretch of basic residues that can be recognized by specialized receptors, transferring signal containing proteins across the nuclear pores. Experiments demonstrated that Archaeal nuclear localization signals motifs can substitute eukaryotic nuclear localization signals to direct intracellular transport of ribosomal proteins in eukaryotic cells, indicating that at least some of them evolved in proteins considerably earlier than the event of cell separation into nucleus and cytoplasm.

Efficient [ribosome] biogenesis requires bigger half of available cellular energy in form of [ATP] and tightly coupled with the energy status of a cell, rendering the process as highly sensitive to nutrient availability.

~**mitochondria**~ |s are centers of energy metabolism in eukaryotic cells; double-membrane organelles:

- **The outer membrane**: permeable to metabolites and small proteins, forms close contacts with the endoplasmic reticulum for the exchange of lipids and [Ca2+], platform for molecular assembly;
-
- **The intermembrane space**: comprised both the space formed by the {cristae} invaginations and the smaller space between the inner boundary membrane and outer membrane;
-
- **The Impermeable Inner Membrane**: comprised of invaginations called {cristae} containing complexes of oxidative phosphorylation system;

A ~**mitohondria**~ contact complexes and {cristae} organizing system, bridging the neck of {cristae} and contact sites in the outer membrane accessing through that to the endoplasmic reticulum complex;

The organization unit of mitochondria genomes consist on mitochondrial DNA in addition to associated architectural proteins, primarily encoding vital subunits of energy generating oxidative phosphorylation stem and electron transport chain the pathway that generates adenosine triphosphate (ATP), a major [~]|energy substrate in eukaryotic cells.

The compact human mitochondrial genome is maternally inherited circular DNA, most likely of bacterial origin [set] of genes encoding genes for 13 proteins of respiratory chain complexes, 2 rRNAs <12S>~<16S>, +22 tRNA.

The mtDNA is transcribed into three long polycistronic precursors~RNAs from 2 strands <heavy>~<light> as the intermix of tRNAs with rRNAs and mRNAs;

~**mitochondria**~ contain an autonomous, spatially segregated genome. Numerous ribonucleoproteins and nucleoprotein complexes self-assemble into non-membrane bound cellular bodies or biomolecular condensates via <liquid>~<Liquid> phase of [separation~aggregation] self-assembly cycles.

Self-assembly is a ubiquitous process for complex systems and can be broadly defined as automatic organization of multiple subunits into ordered multiunit structures; the collective association in multiple elements into more organized configuration, starting from relatively less organized state and evolve, with at least some degree of randomness, into more organized configurations.

Self-organization can create complex systems, aggregates or materials whose properties and functionality raises from their internal structure and/or subunits arrangements; a common scheme is a gradient driven motion: creation of some gradient, whether it be [~], electromagnetic, chemical, thermal,…, across a/the system, existence of sub-components – [particles] which can self-propel over a gradient, sufficiently freely associating/dissociating in the subparts, subsequently resulting in phase separation or aggregate formation, where the subcomponents able to interact through some attractive/repulsive potential, with strength of interactions induced by gradient in the form of available alignment rule~s.

A critical requirement for a target microstructure is a proper balance in the forces for a given system, creation of a focal point in the compact aggregate where subunits can exert a force that can tune mutual interactions through the cooperative arrangements of a forces. The emerging interactions can stabilize emerging structure even in the absence of explicit attractive forces, behaving as active bonds with tunable strength and can be seen as a very selective filters, leading to stabilization of structures influenced by equilibrium condition. For a given gradient: rate of aggregation is proportional to concentration of aggregating subunits;

For a stable/optimal size the dynamics of aggregation can be described as underlying transition between attractive and repulsive forces, influenced by concentration in given particles as a function for a given environment: when concentration of monomers is sufficiently large and sufficiently close to specific level, aggregation became favorable and a system undergoes the sequence of concentration-driven transitions: as the total concentration of interacting subunits increases, the system transitions from monomer dominated equilibrium phase, to a state in which the monomer rich phase is only metastable with respect to aggregate tho assembly does not occur on relevant timescale due to large nucleation energy barrier, to a window of productive assembly and finally to the monomer starvation regime.

At the microscale in the absence of external forces the motion of passive particle is driven by equilibrium fluctuations originated from the environment with much of the dynamics can be described by the theory of Brownian motion and collective behavior can be explained within the framework of equilibrium statistical mechanics.

There are some deviations from equilibrium, for a system may reach, a state of instability in which irregularities or certain components in them tend to grow. When/if this happen a new and stable equilibrium is usually reached with variety in such new equilibriums usually not so great as the variety of irregularities resulted in them.

Combination of imbalances in diffusion rates and interconverting molecular species can lead to compositional inhomogeneities with well-defined, steady state sizes (Turing, 1952):

> a system initially in a stable homogeneous condition, when disturbed from this state by some influence, changes, bringing a system out of the stable state;
>
> a drift away from the equilibrium occurs with almost any big enough displacement from the equilibrium conditions and can be due to change in concentration, or fuel supply, or by a concurrent growth, or be a consequence in change of temperature;
>
> After a lap of time from beginning of instability, a pattern in concentrations appears which can be described in terms of waves;
>
> The chemical wave is achieved whenever is possible and depends on concentrations in the system just beginning to leave a homogeneous condition;
>
> In order to maintain the wave pattern, a continual supply of energy is required, which is supplied through transition of the <fuel substances> into a <fuel products>.
>
> Most of a system|s, most of the time, are developing from one into another; changes take place in the reaction rates.
>
> Under specific conditions the pattern of breakdown of homogeneity is axially symmetric in some new axis determined by the disturbing influence[~]. Growth leads to a difference between two poles of [~]field and [~] gradient driven.

A number of biological mechanisms have been proposed in which assembly sizes are regulated by energy-consuming processes, such as active assembly and disassembly of coupling between protein conformational states and phosphotransferase reactions. [<assembly>/<disassembly>] rates can be modulated by externally controlled gradients in monomer or nucleation factors concentrations.

Microbes ranging from ancient bacteria to eukaryotic organisms are capable of [H~H] (H2 | molecular hydrogen) metabolism. Their ability to either produce or use [H~H] as a metabolite arises from the expression of hydrogenase enzymes.

Hydrogenases are the group of diverse metalloenzymes able to catalyze reversible reaction of dihydrogen into proton and electrons:

$$H2 \leftrightarrows +H{\sim}H\text{-} \leftrightarrows +2H{\sim}2e\text{-}$$

Plasma membrane vesicles are able to utilize [H2] to regenerate [NADH];

Hydrogen accelerates the reversible redox reaction between [NAD+] and [NADH];

The ~**mitochonria**~ the major sites of [NADH] reoxidation into [NAD+] where [NADH] derived electrons are able to enter in the electron transport chain in/for [ATP] production;

[NAD+] or [NADH] cannot pass the mitochondrial membranes and therefore cells evolve mechanisms for substrate cycles use, able to transport the [~]|electrons derived from oxidation cytosolic [NADH] into the ~**mitochondria**~s

The ubiquitous redox coenzyme Nicotinamide Adenosine Dinucleotide (NAD) is incorporated as the very first nucleotide into RNA during transcription initiation by the <RNA Polymerase>~s, acting as the initiating nucleotide, competes with [ATP] at initiating promoters.

The [NAD+] and its metabolites systematically flux and/or exchange across tissues, with a tissue-specific distribution of [NAD+] biosynthetic enzymes and the tissue-specific preference in specific [NAD+] precursors.

The domain wall motion can be controlled by [~]|[field/transfer]: interactions with dynamics in pulses and rhythms of gradients be able to provide a self-consistency condition for antisymmetric interactions influencing the formation of topological structures, subsequently evolving into self-organizing anything is~